

# The Antecedents of Myocardial Infarction and Sudden Death in a Cohort of Actively Employed Men

LAWRENCE E. HINKLE, JR., M.D.

Industrial populations can provide probability samples of actively employed men which can be stratified according to variables such as age, occupation, activity, and medical "risk factors" for coronary heart disease as determined from health records. Career employment and retirement plans make it possible to follow participating subjects over long periods, and to estimate sampling bias by following morbidity and mortality records of designated members of the sample who are unwilling to participate actively. This paper describes the use of such an industrial population in order to determine the incidence of coronary heart disease and sudden death in actively employed middle-aged American men, and to ascertain some of the characteristics of those men who die suddenly and unexpectedly.

*Dr. Hinkle is Director of the Division of Human Ecology of the Departments of Medicine and Psychiatry of Cornell University Medical College, New York, New York.*

*The studies described in this paper were supported by U.S.P.H.S. Grant HE-07796.*

*Presented at the 56th annual meeting of the Industrial Medical Association in Atlanta, Ga., April 19-22, 1971.*

## Methods

This investigation was based upon a prospective and retrospective study of an age cohort of men drawn from the New Jersey Bell Telephone Company in 1962. The operations of this company cover rural, urban and metropolitan areas in roughly equal proportions. The 10,000 men on its payroll in 1962 were divided into occupational categories parallel to and essentially identical with those used throughout other units of the Bell System. Over the period of the study, the annual age-specific death rates for coronary heart disease between the ages of 30 and 60 are not significantly different from those reported for all American men.<sup>1</sup>

The cohort was selected by obtaining a complete payroll of the company for January 1, 1935, and then designating all of those men on the list who had been born between January 1, 1902, and December 31, 1908, and who had been hired between January 1, 1923, and December 31, 1930. In all, 1,160 men were designated by this procedure. Of these, 274 had had college degrees when hired, and 886 had not.

The 30-year experience of these men was traced by various means. Since the great bulk of them had remained on the payroll of this company, had retired from this company, or had been transferred to other companies within the industry, the industrial records provided an immediate means of determining their present status, as well as their employment history. The company possessed similar information on all those who had died while on the active payroll, and on all of those who had died after retirement. A total of 1,066 men were located from the company records.

Ninety-four of the men in the cohort, or 8.1 per cent of the total, had resigned or had been dismissed at some time between January 1, 1935, and January 1, 1965. Most of these resignations or dismissals occurred in the period between 1935 and 1940. It was possible to obtain the Social Security numbers of 61 of these men. These were submitted to the Division of Claims Policy of the Social Security Administration, which supplied us with data on all of those for whom death claims had been filed, including the data and place of filing. Of the remaining 33 men, all except eight (six "no college" men and two "college" men) were located by information obtained from telephone directories, from college Alumni Associations, and from friends and relatives.

Of the 1,152 men whose status on January 1, 1965, was ascertained, 166 had died. Copies of the death certificates for all of these men were obtained. Extensive company medical records were still available for 40 of them, and it was possible to compare these with the data on the death certificates (Table I).

In 1962 we selected a random sample of 301 men of median age 55, who were then on the active payroll of the New Jersey Bell Telephone Company (Table II). This was a sample of all men in this age cohort who were then on the payroll of the company, stratified so

as to insure adequate representation of all major occupational categories.<sup>1</sup> These men were examined and studied in terms of their physical characteristics, electrocardiograms, chest x-rays, serum lipids, and smoking and dietary histories and psychological and social characteristics. From each of these men we obtained a sample of 20,000 to 30,000 cardiac complexes by monitoring their electrocardiograms over a six- to seven-hour period of carefully standardized activities between 8:30 A.M. and 4:30 P.M. The routine included various changes of position, graded levels of physical activity, the effects of ingesting hot and cold fluids, and of a large meal, and the effects of exposure to interviews and psychological tests which were anxiety-producing for some men. The electrocardiographic data were obtained with portable tape recorders (Holter Avionics Electrocardiocoder) after the voltage and timing characteristics of these devices had been carefully ascertained and arrangements had been made to offset some of the inherent limitations of this equipment.<sup>2</sup> The routine was stop-watch timed and guided by a technician. From the 301 subjects, 268 complete records suitable for analysis were obtained. Incomplete or partly defective records were obtained on many of the remaining subjects.

In order to analyze these data a complete photographic write-out of the R-R intervals was prepared<sup>3</sup> on which the time of each activity was precisely located. From this record heart rates under various conditions could be calculated, and all potential changes in rhythm and potential dysrhythmias could be identified. These were investigated by scanning them at real-time and by real-time write-out of the complexes.

The examination of these men and the initial collection of the electrocardiographic data were completed in 1963 and 1964. After that the entire group was followed carefully and data were obtained on all deaths and disabilities. In 1967 a schedule of re-examining was begun. This was accompanied by a 24-hour monitoring, yielding samples of approximately 120,000 complexes. The longer records were obtained after it became evident that many important changes in rate and rhythm occurred in the evening and during the course of sleep.

The second examinations were completed in December 1969. After that all men who had not been examined for a second time because they were disabled, or because they had moved away from the area, or for any other reason, were contacted by telephone. The interval histories of these men were reviewed with them, and it was arranged that those nearby would have electrocardiograms and measures of their blood pressures at their homes by our technicians. Men living in other states had electrocardiograms and blood pressure measurements performed by their private physicians, who were contacted by us, instructed in our methods of carrying out these

TABLE I  
THE AGE COHORT  
STATUS OF MEN ON JANUARY 1, 1965

1160 men in original cohort
790 men still on payroll of original company
33 men transferred to other companies, living
90 men retired, living
73 men resigned or dismissed before age 45, living
8 men not accounted for
166 men dead
Thirty-year death rate, 144.2 per 1,000

TABLE II  
A STRATIFIED RANDOM SAMPLE OF ALL ACTIVELY  
EMPLOYED MEN AGED 55-60 ON THE PAYROLL OF ONE  
COMPANY

79 workmen	46 foremen
86 supervisors	90 managers
Total—301 men	

procedures, and were paid a small fee for their services.

At follow-up, information was obtained on the condition of all of the men in the original sample (Table III). Of those originally examined, 214 men (71.1 per cent) returned for a second complete examination and 24-hour recording. Twenty-seven men died before they could be re-examined; 60 men could not be re-examined (20 because they were disabled and unable to make the trip to New York, 11 because they had moved to other parts of the country, and 25 for "personal reasons"—chiefly because their wives or other members of their families were disabled and they had no one to leave them with, or because they themselves felt that the trip to New York and a day of examination would cause them too much discomfort or inconvenience). All except four of these men reviewed their histories with us and allowed us to obtain blood pressure readings and electrocardiograms. In four instances we knew only the health record of the man until he retired from the company, and we knew that he was still alive at the time that this report was prepared.

Results

*Status of the Men in the Cohort on January 1, 1965:* The status of these men on January 1, 1965, is shown in Table IV. Those remaining on the payroll 30 years after the date of designation numbered 790, or 68.1 per cent of the original cohort. Their median age was 60 years at this time. The biggest single cause of attrition in the group during the intervening years was the death of men on the active payroll. Most of the retirements had occurred among men past the age of 55; the bulk of them were among men age 60 or older. Most of those transferred to other companies in the industry had remained on the active payroll. Only 8.1 per cent of the

TABLE III  
FOLLOW-UP INFORMATION OBTAINED

	No.	% of Total
Initial examination, 1963-1964		
Men examined	301	100
Complete recordings	283	94.0
Number of complexes/complete recording	30,272 ± 644.8	
Died before second examination	27	9.0
Second examination, 1967-1969		
Examined completely with 24-hour recordings	214	71.7
Interval history, standard ECG and BP only	56	18.6
Data from company only	4	1.3

TABLE IV  
STATUS OF MEN IN  
COHORT ON JANUARY 1, 1965

	Living 1/1/1965	Died Before 1/1/65	Rate per 1,000
On payroll, this company	790	136	146.9
Transferred to other companies	33	2	57.1
Retired	90	15	142.9
Resigned after 1/1/35	48	8	142.9
Dismissed after 1/1/35	25	5	166.7
Totals	986	166	144.2

original cohort had dropped out of the industry entirely. These findings were in accord with the evidence from other sources which indicated that the nationwide industry experiences relatively little attrition among men between the ages of 30 and 60 for causes other than death.

*The Thirty-Year Experience—Death by Cause:* Of the 1,152 men whose status on January 1, 1965, was ascertained, 166 had died, yielding an over-all death rate of 144.2 per thousand for the 30-year period. The death rates for the men who had retired, resigned, or had been dismissed were comparable to the death rates of those who had remained on the payroll of the company (Table IV).

The most frequent single cause of death among the men in this cohort in the years from ages 30 to 60 was "coronary occlusion" or "myocardial infarction," so specified on the death certificate. This accounted for 65 deaths with a rate of 56.4 per thousand (Table V). The rate for cardiovascular disease was 82.5 per thousand for the 30 years. Various forms of cardiovascular disease accounted for more than half of the deaths in the cohort.

Neoplasia was the second most frequent cause of

TABLE V  
DEATHS OCCURRING AMONG 1,152 MEN BETWEEN  
AGE 30 AND AGE 60 BY CAUSE

	Deaths	Rate per 1,000
"Coronary occlusion" and "myocardial infarction," so specified	65	56.4
Other heart disease	15	13.0
Vascular disease	14	12.1
Neoplasia	36	31.3
Infection	14	12.1
Suicide	6	5.2
Accidents	6	5.2
Various other conditions	10	8.6
Totals	166	144.2

TABLE VI  
DEATHS AMONG MEN ON PAYROLL AND MEN PREVIOUSLY TRANSFERRED, RETIRED, RESIGNED AND DISMISSED

	On Payroll		Not on Payroll	
	Deaths	Rate per 1,000	Deaths	Rate per 1,000
Total deaths	136	146.9	30	132.7
Coronary deaths	54	58.3	11	48.7

death. Various infectious processes, some localized or secondary to injuries, accounted for 14 deaths, predominantly in the younger age ranges. Suicides and accidents were relatively frequent causes of death in the younger ages, also.

The coronary heart disease death rate for men who had been separated from the payroll for various reasons was essentially the same as the rate for the men who had remained on the payroll (Table VI).

*The Prevalence of Coronary Heart Disease Among the Survivors Still on the Payroll:* After an appropriate adjustment for sampling proportions, the prevalence of overt coronary heart disease among the 856 survivors who were on the payroll when the sample was drawn was estimated at 14.8 per hundred (Table VII). Since the cohort had already lost 5.6 men per hundred from coronary heart disease before the sample was drawn, the 30-year prevalence of overt coronary heart disease during the period between ages 30 and 60 may be estimated at 20.4 per hundred. In effect, one man in five developed definite evidence of coronary heart disease during this time.

*The Prevalence of Risk Factors in the Selected Sample:* The original sample of 301 men was found to include 10 men who had sustained previous definite myocardial infarctions, 29 with other definite evidence of coronary heart disease (Princeton Conference Criteria),<sup>4</sup> and 19 men with otherwise unexplained definite abnormalities of the ST segments and T waves

on their standard electrocardiograms, or with chest pain described as “probable,” but not “definite” angina pectoris (Fig. 1). The remaining 204 men, who had no definite evidence of coronary heart disease, were ranked according to the number of “risk factors” which they exhibited, and the apparent severity of these. The risk factors that we utilized were those that were understood to be important in 1962 when the study was initiated (e.g., the level of blood pressure, LVH on the standard ECG, left ventricular prominence on the chest x-ray, level of cholesterol, the presence of diabetes mellitus, evidence of atherosclerosis in other arteries, and the ponderal index). Fifty-eight men with hypertension greater than 160/95, left ventricular hypertrophy patterns on ECG, serum cholesterol levels above 300 mg %, diabetes mellitus, or combinations of these and similar variables were regarded as a “high risk group.” The next 175 men were ranked in groups according to the extent to which they exhibited risk factors of a lesser degree. There were only nine men in the sample of 301 who were slim, with normal blood pressure, normal blood lipids, entirely normal ECG’s, and no evidence of any other risk factors.

**Clinical Characteristics of the Men Who Died:** Twenty-four of the 301 men in the sample were reported on their death certificates as dying of coronary heart disease before December 31, 1970. Sixteen of these men died between 1963 and 1968, after our initial examination, but before the second examination could be performed. The time between the first examination and their deaths ranged from four months to five and a half years. Eight men survived for five years after the first examination, were re-examined in 1967-69, and then died before the end of 1970. The time between the second examination and the deaths of these men ranged from three months to 23 months.

Twelve of the men who died had clinical coronary heart disease (Princeton Conference Criteria) at the time of their first examination. Three others developed clinical coronary heart disease before their fatal episode (Table VIII).

Six of these men had hypertensive cardiovascular disease with LVE on x-ray, or LVH on ECG. Ten had chronic bronchitis or emphysema. Seven had diabetes mellitus. Two had clinical gout, and eight had serum uric acid levels  $\geq 7.0$  mg% (enzymatic method). (Three of these may have been receiving thiazides as treatment for hypertension). One man had serum cholesterol  $\geq 300$  mg%, and two had serum triglycerides  $\geq 200$  mg%. Eight men were judged to be “obese” on clinical grounds. Five had ponderal indices  $\leq 12.00$ . Nineteen of the 24 had smoked cigarettes for more than 30 years. Seven were still smoking two packs of cigarettes per day at the time that they were examined.

On clinical grounds alone, if one had had to characterize these men as they appeared at the last examination before they died, one might have said the following:

TABLE VII  
CORONARY HEART DISEASE SURVIVORS  
ON PAYROLL

Manifestation	Rate per 100 (Adjusted for Sampling Proportions)	Estimated Total Cases Among Survivors
Previous myocardial infarction		
(1) "Definite" by history and record	4.5	38
(2) "Probable" by history and record	1.5	13
(3) ECG evidence only	2.1	18
Angina pectoris, typical by history	3.4	29
Coronary insufficiency by history and record	3.3	29
Total of above	14.8 (11-20)*	127 (94-171)*
ST and T abnormalities on ECG, otherwise unexplained	6.3 (3.8-9.6)*	54 (33-82)*

\* Approximate 5% confidence limits

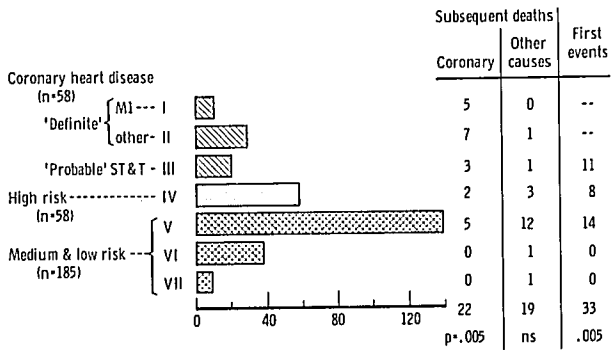


Fig. 1.

Ten of them were men whose primary illness was coronary heart disease (Nos. 87, 120, 138, 141, 157, 21, 332, 92, 28, 31); five of these men with coronary heart disease also were obese or diabetic or both (Nos. 87, 141, 332, 28, 31).

Two men had coronary heart disease, but they also had chronic bronchitis and emphysema, and were obese (Nos. 328, 343).

Three were men whose primary illness was hypertensive cardiovascular disease, although they had some evidence of coronary heart disease also (Nos. 48, 89, 259); one of these three was obese, one was a diabetic and two had chronic bronchitis and emphysema.

Three of these were men whose primary illness appeared to be hypertensive cardiovascular disease and LVH, essentially uncomplicated (Nos. 115, 135, 101).

One man was a hypertensive with some emphysema (No. 303).

TABLE VIII  
24 MEN WHO DIED—  
CLINICAL FINDINGS AT LAST EXAMINATION PRIOR TO DEATH

Code No.	Pre-Existing		CHD		Hypertension		Lung Disease	Diabetes Mellitus	Clinical Gout	SUA ≥7.0 mg	Chol. Tri.	Clin. Obesity	P.I. ≤12.0	Now Smoking
	Clin. MI	ECG Ev.	CI or AP	BP	LVH or LVE									
87	MI	—	CI	AP	—	—	—	Diabetes	—	—	—	—	—	1 pk.
120	MI	—	—	—	—	—	—	—	—	8.1	—	—	—	—
138	MI	—	CI	AP	Def.	—	—	—	—	—	—	—	—	—
141	MI	—	—	—	Bord.	—	—	Diabetes	Gout	—	—	Obese	—	—
157	MI	—	—	AP	Bord.	—	—	—	—	—	—	—	—	—
21	—	—	CI	AP	Bord.	—	—	—	Gout	8.6	—	—	—	—
48	MI	—	CI	AP	Def.	LVE	—	—	—	7.0	—	Obese	—	—
89	—	ECG	CI	AP	Def.	LVH	Emphy. Bron.	Diabetes	—	8.5	442/210	—	—	2 pk.
259	—	—	CI	AP	Def.	LVH	Chron. Bron.	—	—	—	—	—	—	—
328	—	—	—	AP	—	—	Chron. Bron.	—	—	—	—	Obese	—	2 pk.
332	—	ECG	—	—	Bord.	—	—	—	—	—	215/207	Obese	11.2	2 pk.
343	—	—	—	AP	Def.	—	Emphy.	—	—	10.0	—	—	12.0	—
30	—	—	—	—	—	—	Emphy.	—	—	—	—	Obese	11.2	—
115	—	—	—	—	Def.	LVH	—	—	—	—	—	—	—	—
135	—	—	—	—	Def.	LVH	—	—	—	—	—	—	—	—
55	—	—	—	—	—	—	Emphy.	—	—	—	—	—	—	1 pk.
92	MI	—	—	AP	Bord.	—	—	—	—	—	—	—	—	2 pk.
221	—	—	—	—	Bord.	—	Emphy.	Diabetes	—	—	—	—	—	2 pk.
28	—	ECG	—	—	Bord.	—	—	Diabetes	—	—	—	Obese	—	—
31	—	—	—	AP	Def.	—	—	Diabetes	—	8.2	—	—	—	—
101	—	—	—	—	Def.	LVH	—	—	—	16.5	—	—	—	2 pk.
275	—	—	—	—	Bord.	—	Bron. Emphy.	—	—	8.5	—	Obese	11.9	2 pk.
303	—	—	—	—	Def.	—	Chron. Bron.	—	—	—	—	—	—	—
334	—	—	—	—	Bord.	LVE	Bron. Emphy.	Diabetes	—	—	—	Obese	—	1 pk.

\*Abbreviations:  
MI, myocardial infarction  
ECG, ECG evidence of myocardial infarction (QRS criteria)  
CI, coronary insufficiency  
AP, typical angina pectoris  
LVE, left ventricular enlargement on chest x-ray (C/T  $\geq 50\%$ )  
LVH, left ventricular hypertrophy pattern on standard ECG

Hypertension: Def., blood pressure  $\geq 160/95$   
Bord., blood pressure 140-159/90-94  
SUA, serum uric acid  
Chol., cholesterol  
Tri., triglyceride  
PI, ponderal index

Four of these men primarily had chronic lung disease (Nos. 30, 55, 275, 334). One of them (No. 55) may have been concealing angina pectoris; one (No. 221) was also an alcoholic; two (Nos. 275 and 334) were obese; two (Nos. 221 and 334) were diabetic; and one (No. 334) probably had cor pulmonale.

In short, none of these 24 men was without clear-cut readily diagnosable coronary heart disease, hypertensive cardiovascular disease, or chronic

obstructive pulmonary disease at the time of the last examination before his death. Most of these men had some combination of these three conditions, usually accompanied by significant metabolic disease also.

In spite of this, the physicians who attended eight of these men on an emergency basis immediately before or after their deaths seemed to have thought that these men had previously been essentially healthy or asymptomatic. Many of their associates had regarded

TABLE IX  
24 MEN WHO DIED—CLINICAL CHARACTERISTICS OF THE FATAL EPISODE

Code No.	Prior Clinical CHD	Report of Premonitory Symptoms	Duration of Final Eps.	Clinical Characteristics of Final Eps.	Clinical Characteristics of Death	Estimated Mechanism of Death	Autopsy
87	Yes	None	3 days	Acute MI	Grad.—hours	Pump fal.	Rec. MI
120	Yes	None	1 hr	Acute MI	Grad.—1 hr	Pump fal.	—
138	Yes	None	3 hr	Acute MI	Abrupt	Arrhy.	—
141	Yes	None	Minutes	"Sudden death"	Abrupt	Arrhy.	—
157	Yes	None	Minutes	"Sudden death"	Abrupt	Arrhy.	—
21	Yes	None	8 hr	Acute MI	Abrupt	Arrhy.	—
48	Yes	Chest pain—1 day	Minutes	"Sudden death"	Abrupt	Arrhy.	—
89	Yes	Breathlessness	4 days	Cong. ht. fal.	Abrupt	Arrhy. (doc.)	—
259	Yes	None	1 day	Acute MI	Abrupt	Arrhy. (doc.)	—
328	Yes	None	Minutes	"Sudden death"	Abrupt	Arrhy.	—
332	Yes	None	7 days	Acute MI	Grad.—4 hr	Pump fal.	—
343	Yes	None	½ hr	Acute MI	Grad.—½ hr	(?)Pump fal.	Rec. MI
30	—	Breathlessness	Hours	Acute resp. fal.	Gradual	Pump fal.	—
115	—	None	Minutes	"Sudden death"	Abrupt	Arrhy.	Old MI
135	—	None	1 hr	Acute MI	Grad.—1 hr	(?)Pump fal.	—
55	—	None	Minutes	"Sudden death"	Abrupt	Arrhy.	—
92	Yes	None	Minutes	"Sudden death"	Abrupt	Arrhy.	—
221	—	None	1 day	"Sudden death"	Unknown	Prob. arrhy. or pump fal.	—
28	Yes	None	Minutes	"Sudden death"	Abrupt	Arrhy.	—
31	Yes	None	Minutes	"Sudden death"	Abrupt	Arrhy.	Fresh clot in rt. cor. art.
101	—	None	10 min	"Sudden death"	Abrupt	Arrhy.	Cor. athero. LVE
275	—	None	Minutes	"Sudden death"	Abrupt	Arrhy.	—

\*Pump fal., pump failure  
Arrhy., arrhythmia  
Doc., documented

them as essentially healthy also. Thus, from the point of view of many of those in attendance at the last fatal episode, these were "unexplained sudden deaths in apparently healthy men."

*The Nature of the Fatal Episode:* At the time of the fatal episode, 15 of the 24 men were known to have clinical coronary heart disease. Nine were not (Table IX).

Twenty-one of the group were regarded by their families, their associates, and their physicians as being in their usual state of health shortly before the fatal episode developed. If they had any premonitory symptoms indicating that they were about to become acutely ill, they did not report these to their physicians or to the people around them. One man (No. 48) had intermittent chest pain for one day prior to his last episode; and two men, (Nos. 89 and 30) apparently experienced increased breathlessness for some time before they began to regard themselves as acutely ill. There were two men who had been under treatment for chronic congestive heart failure, but there was no report that they had experienced any acute symptoms

until their final illness occurred. So far as it was reported to us, none of the men had any premonition of death.

Eleven men died within minutes after the onset of their fatal episode with a syndrome that might be called "sudden and unexpected death." Seven of these men were known to have coronary heart disease; four were not so known.

Four men died within an hour or less after the onset of their fatal episode. One of these (No. 101) experienced a sudden and unexpected death within a period of no more than 20 minutes. Three others had symptoms and signs of an acute myocardial infarction with severe pain, collapse, and death within one hour or less.

Six men had final episodes which lasted more than an hour, but less than a day. Three of these men (Nos. 138, 21, 259) had symptoms and signs of an acute myocardial infarction. One man (No. 30) died in the setting of a typical and severe episode of acute respiratory failure. Another (No. 334), who had some chronic lung disease and who had an acute upper

respiratory infection with some evidence of respiratory failure, died overnight, in his bed, unobserved. Another (No. 221), an alcoholic with chronic bronchitis and emphysema, was last seen, apparently in his usual state of health, on the evening before he was found dead.

Three men experienced final episodes of illness which lasted more than one day. One (No. 87) died three days after the onset of an acute myocardial infarction; one (No. 332) died seven days after an acute myocardial infarction and four hours after a recurrence of his pain, with signs suggesting that an extension of the infarct had occurred. One man (No. 89) died four days after he was admitted to a hospital for treatment for acute congestive heart failure.

If one assumes that when a man is at home or at work, one hour would be an average minimal delay time from the onset of the first symptoms of illness to the institution of effective medical treatment administered by trained personnel, then it is reasonable to say that 15 of these 24 men died so rapidly that such medical treatment after the onset of the fatal event was essentially impossible.

The clinical characteristics of the fatal episode of 12 of these men were those of an abrupt and unexpected death in men who had not appeared to be acutely ill a few minutes before the episode began. At one moment in time these men were busy with their usual activities—driving an automobile, sitting in a chair, riding in a bus, sleeping, or playing golf. Minutes later they had collapsed and died. Even when a physician was as near at hand as the next tee on the golf course, he found the patient pulseless and apparently dead upon his arrival (Table IX).

Eight other men died during the course of illnesses having the clinical characteristics of an acute myocardial infarction. One died during the course of an acute exacerbation of chronic congestive heart failure. Another died in the setting of acute respiratory failure, and two died unexpectedly in their beds, whether abruptly or gradually is not known.

The final agonal moments of 17 of these men were characterized by an abrupt collapse. In some instances this was observed from its onset by people who were nearby, and it was described vividly by them. Three men died in this manner while they were under treatment in hospitals for acute myocardial infarctions. Another died while under treatment for congestive heart failure, and 12 died in this manner when they were active and in no apparent distress. In addition to these, four men died gradually with symptoms suggesting increasing cardiovascular collapse, and two others probably died in this manner. Nothing is known about the final moments of two of these men.

It was our estimate that probably 17 of these men died because of the development of a dysrhythmia or cardiac standstill. Five others apparently died of pump failure, and two may have died in either manner.

*Cardiac Rhythm:* Analysis of the original samples of

electrocardiographic data indicated that transient or prolonged disturbances of cardiac rhythm or conduction were extremely common in this sample of middle-aged men, during six hours of ordinary activity, and that these were largely asymptomatic.<sup>3</sup>

All except 22 of the men in the sample had transient dysrhythmias. Supraventricular dysrhythmias were most common. In all, 76.1 per cent of the men displayed one or more supraventricular premature contractions during the course of the six-hour recording period. Nearly all of these were atrial in origin. A total of 12.8 per cent exhibited one or more supraventricular premature contractions per 1,000 complexes, and 6.4 per cent exhibited 10 or more supraventricular premature contractions per 1,000 complexes. There were 11 men with episodes of bigeminy, 9 men with episodes of trigeminy, 34 men who had paired SPC's, and 13 men who had multiple consecutive SPC's, as well as 2 men who had episodes of paroxysmal supraventricular tachycardia. In general, complex supraventricular dysrhythmias occurred in men who had frequent supraventricular premature contractions.

One man had a transient paroxysmal nodal tachycardia. Some others had transient episodes of tachycardia which may have been either nodal or ventricular in origin.

Ventricular dysrhythmias were almost as common as supraventricular dysrhythmias, occurring in 176 records in the sample. One man had a ventricular parasystolic rhythm. There were 80 men who had one or more VPC's per 1,000 complexes. In all, 94 men had VPC's from two or more foci, 24 had episodes of ventricular bigeminy, 17 had episodes of trigeminy, 36 had paired VPC's, and 9 men had runs of three or more consecutive ventricular beats—apparently “paroxysmal ventricular tachycardia,” although it cannot be ruled out that some of these may have been paroxysmal nodal tachycardias. In general, complex ventricular dysrhythmias occurred in men with many VPC's.

The presence of frequent ventricular dysrhythmias ( $\geq 10$  VPC's per 1,000 complexes) was significantly associated with subsequent coronary death (25 men, 7 deaths,  $P < .005$ ).

*Cardiac Conduction:* Asymptomatic disturbances of intracardiac conduction were also quite common in this sample.<sup>3</sup> There were seven men with first degree A-V block ( $PR \geq .21$  seconds). The mean PR time for all men was  $.1622 \pm .0026$  seconds. Twelve men had PR intervals of .12 or less. One of these men had an identifiable A-V nodal rhythm. In one man, 2:1 A-V block occurred. It was intermittent and it was not present at the time that the standard electrocardiogram was obtained.

Fifty-four men had intraventricular conduction defects.<sup>3</sup> Thirty-two of these men had QRS times  $\geq .10$  seconds. Seven men had RBBB. Two men had LBBB. Four men had  $S_1S_2S_3$  patterns with QRS  $\geq .10$  seconds. Nineteen other men, with QRS  $\geq .10$  seconds, were identified only as having IV blocks. Eight of these were

constant, and 11 were transient. In addition, there were 22 men who had abnormalities of IV conduction without prolonged QRS times. Sixteen of these men had  $S_1$   $S_2$   $S_3$  patterns with or without an  $RSR_1$  in  $V_1$  and six men had only an  $RSR_1$  in  $V_1$ .

The presence of conduction defects was significantly associated with subsequent coronary death (54 men, 11 deaths,  $P < .005$ ).

**ECG Evidence of Myocardial Infarctions, Ischemia, Axis Deviation, and LVH:** In addition to these abnormalities of rhythm and conduction, many men showed other significant electrocardiographic abnormalities. Eight men had QRS abnormalities indicative of a previous myocardial infarction. Twenty-six men had "ischemic" ST segments and T waves. Twenty-seven men had leftward deviation of the QRS axis ( $\geq -30$  degrees), and 20 men had LVH patterns on the standard ECG. All of these phenomena were significantly associated with subsequent coronary death.

**Heart Rates:** Significant abnormalities of heart rate also were encountered among the men in this sample.<sup>5</sup>

The standard procedure that was utilized made it possible to study their heart rates over the six-hour period. Men who died subsequently of coronary heart disease had consistently lower mean heart rates than those who survived. Their morning supine heart rate was slow, their heart rates did not rise greatly during the day, and their mean afternoon heart rates were significantly lower than those of other men in the sample. We have referred to this phenomenon of persistent slow heart rate with a low peak rate response to exercise as "sustained relative bradycardia."<sup>5</sup> It appears to be significantly associated with disorders of cardiac conduction. In this sample it has also been significantly associated with subsequent coronary death.

A second apparently significant abnormality of heart rate has been a sustained tachycardia. We have found this to be associated with the presence of hypertension, but its association with subsequent coronary death has been only a weak one.

**Conclusions:** Several tentative conclusions have been drawn from this original study, and have been set up as hypotheses to be tested in the studies that are now under way. These include the following.

1. Middle-aged men whose deaths are reported as due to "coronary heart disease," including those with sudden and unexplained deaths, are not drawn from the population of apparently healthy men. "Coronary deaths" occur among a mixed population of men with what appears, on clinical examination, to be coronary heart disease, hypertensive cardiovascular disease, and chronic lung disease, or some combination of these conditions; and the majority of men who die "coronary deaths" also have one or more significant metabolic abnormalities such as hyperlipidemia, impaired glucose tolerance, elevated serum uric acid, obesity, and alcoholism. Many are heavy smokers. Many of the

physiological abnormalities and pathological conditions of men who die "coronary deaths" would be detectable if the subject were examined within two to three years prior to his death.

2. Men who are reported as dying from coronary heart disease, including those who die suddenly and unexpectedly, have abnormalities of cardiac rate, rhythm and conduction prior to the onset of their fatal episode. This can be detected by standard electrocardiograms and by 24-hour taped records of their electrocardiograms obtained under standard conditions of position, activity, food intake and sleep.

3. Phenomena which may be found in the taped records of the electrocardiograms of middle-aged men, and which carry with them a substantial risk of death in the next five years, include: (1) VPC's occurring at a frequency of 10 per 1,000 complexes or greater; (2) intraventricular conduction defects, constant or transient, especially if associated with prolongation of the QRS time beyond .10 seconds; (3) sustained relative bradycardia, as defined above, especially if this is associated with evident abnormalities of rhythm or conduction, or if it occurs in the presence of clinical coronary heart disease.

**Acknowledgments:** The author wishes to express his gratitude to Dr. George Bisgeier, Medical Director of the New Jersey Bell Telephone Company, and to the employees of that company for their invaluable assistance, without which this study would not have been possible. He also wishes to acknowledge the collaboration of Bry Benjamin, M.D., William N. Christenson, M.D., Edward W. Lehman, Ph.D., Dorothy S. Ullmann, B.S., Susan T. Carver, M.D., Arlene Plakun, M.A., and Michael Stevens, among others, who participated in the examination of these men and in the collection of the data.

*Cornell University Medical College  
525 East 68th St.  
New York, N.Y. 10021*

## References

1. Hinkle LE, Benjamin B, Christenson WN, et al: Coronary heart disease: the thirty-year experience of 1,160 men. *Arch Environ Health* 13:312-321, 1966
2. Hinkle LE, Meyer J, Stevens M, et al: Tape recordings of the ECG of active men: limitations and advantages of the Holter-Avionics instruments. *Circulation* 36:752-765, 1967
3. Hinkle LE, Carver ST, Stevens M: The frequency of asymptomatic disturbances of cardiac rhythm and conduction in middle-aged men. *Amer J Cardiol* 24:629-650, 1969
4. Epidemiology of cardiovascular disease methodology. American Heart Association—National Heart Institute. *Amer J Public Health* 30:10, 1960
5. Hinkle LE, Carver St, Stevens M, et al: Phenomena of heart rate associated with coronary heart disease, hypertension and coronary death. Presented at the 43rd scientific sessions of the American Heart Association, Atlantic City, N.J., on November 13, 1970 (In preparation)